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Cbfβ/Runx1 complex is important for articular cartilage integrity

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Osteoarthritis (OA), a leading age-related disease in society, still lacks a clear molecular mechanism. Here, we explored in vivo role of core binding factor β (Cbfβ) in OA by generating articular cartilage-specific Cbfβ-deleted mice (Cbfβ□ac/□ac) using Gdf5 promoter-driven Cre mice. OA was induced through destabilization of the medial meniscus (DMM) surgery in 12-week-old male mice. At 8 weeks after surgery, OA phenotypes were more accelerated in Cbfβ□ ac/□ ac mice than wild type (WT) mice with increased expression of Mmp13 and decreased expression of Type II collagen. Interestingly, the expression of Cbfβ was reduced during aging as determined by immunohistochemisty. Furthermore at 5 months of age Cbfβ□ac/□ac mice, but not in WT, exhibited OA naturally without developmental defects in joint and skeletal tissue formation. To explore the molecular mechanism of the protective role of Cbfβ in OA, we measured the expression of chondrocyte markers, Runx transcription factors, and Cbfβ in articular cartilage. Expression of chondrocyte markers such as type II collagen, Aggrecan, and Cbfβ was attenuated in chondrocytes derived from Cbfβ□ac/□ac OA mice compared to WT mice. Among Runx family, Runx1, but not Runx2 and Runx3, was highly expressed in particular chondrocytes. Expression of Runx1 was gradually decreased during OA progression in WT mice. Importantly, Runx1 expression was further diminished in Cbfβ□ac/□ac OA mice. Cbfβ formed a complex with Runx1 and protected Runx1 from proteosomal degradation in primary articular chondrocytes as well as in ATDC5 cells. Consistently, forced expression of Cbfβ in Cbfβ-deficient primary articular chondrocytes restored the chondrocyte markers and Runx1 expression. Collectively, these results demonstrate that Cbfβ is required for Runx1 stability as a partner protein in articular cartilage and that the formation of the Cbfβ-Runx1 complex plays an essential role for maintenance of articular cartilage integrity.

Biography

Xian Jin is currently working as young researcher at Kyungpook National University, Korea

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